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CASE REPORT
Arrhythmias/electrophysiology

Paradoxical cardiac conduction during exercise stress testing in myotonic dystrophy type 1: a case report

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Background Exercise stress testing (EST) identifies functional abnormalities that may manifest only during physiologic stress to the heart. This may have significant prognostic value in identifying latent conduction abnormalities in asymptomatic patients with myotonic dystrophy type 1 (MD1), who may benefit from prophylactic permanent pacemaker (PPM) implantation.

Case report We report the case of a patient with MD1 with a 5-month history of atypical left-sided chest pain. Her baseline electrocardiogram (ECG) showed sinus rhythm and variable PR interval prolongation (206–220 ms) without symptoms of cardiac conduction disease. Routine blood tests and cardiac investigations including a 24-h ECG monitoring, echocardiogram, and a cardiac magnetic resonance imaging scan, revealed no abnormalities. To investigate her chest pain and to determine the need for prophylactic PPM implantation, EST and an electrophysiological study were performed. Exercise testing revealed minimal PR shortening (PR = 200 ms) at peak exercise and paradoxical PR prolongation (PR = 280 ms) during the early recovery period. A prophylactic DDDR PPM was implanted following an electrophysiological study that revealed a prolonged His-ventricle (HV) interval of 84 ms.

Discussion The current use of annual ECG and 24 Holter monitoring may not adequately detect abnormal cardiac conduction in asymptomatic patients with MD1. The invasive nature of electrophysiology studies limits its use as a screening tool for conduction abnormalities in asymptomatic patients. Thus, EST could be used to identify underlying conduction abnormalities in MD1 patients without any specific symptoms of bradycardia, which warrant further invasive electrophysiological studies (EPS).

Keywords Myotonic dystrophy type 1 • Electrophysiology study • Permanent pacemaker • Exercise stress testing • Case report

Introduction

Myotonic dystrophy type 1 (MD1) is an inherited autosomal dominant neuromuscular disease caused by microsatellite (CTG) expansions, with the number of microsatellite repeats correlating with disease severity.[1] Clinically, MD1 is characterized by progressive muscle wasting, ocular, and endocrine disease. In addition, progressive cardiac conduction disease and/or ventricular arrhythmias affect the majority of patients with MD1 and are major causes of sudden cardiac death (SCD).[2]

Permanent pacemaker (PPM) implantation is recommended in MD1 patients who have evidence of second-degree, third-degree

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Learning points

- Annual electrocardiogram and Holter monitoring in asymptomatic patients with myotonic dystrophy type 1 (MD1) may fail to identify cardiac conduction abnormalities.
- MD1 patients with adequate physical exercise capacity who do not exhibit any specific symptoms of bradycardia may benefit from annual exercise stress testing.
- To identify latent conduction abnormalities. This may identify patients in whom confirmatory electrophysiology study (EPS) may not have been considered otherwise.
- Our understanding regarding the genotype–phenotype correlation continues to evolve in patients with MD1 and other neuromuscular disorders. Thus, it is imperative to be aware of the current guidelines and updates made regarding this group of patients.
- EPS remains the gold standard test for excluding significant conduction disease in MD1.

atrioventricular (AV) block or an His-ventricle (HV) interval of ≥70 ms on an electrophysiology study (EPS), regardless of symptoms.[3,4] Prophylactic PPM implantation is also recommended in MD1 patients with first-degree AV block (PR >240 ms), QRS >120 ms, or fascicular block in contrast to the guidelines for patients without neuromuscular disease. In addition, implantable cardiac-defibrillator implantation is recommended in patients with sustained ventricular arrhythmias.[3]

We report a case of an MD1 patient without any specific symptoms of bradycardia and borderline PR interval prolongation who developed abnormal cardiac conduction during exercise stress testing (EST) requiring prophylactic PPM implantation.

Timeline

Date	Event
June 2018	Referral to Cardiomyopathy Clinic. Electrocardiogram (ECG): Sinus Rhythm, PR = 220 ms, borderline left anterior fascicular block (LAFB)
August 2018	Initial assessment. ECG: Sinus Rhythm, PR = 223 ms, LAFB. Prophylactic permanent pacemaker (PPM) discussed
September to December 2018	24-h ECG monitoring, echocardiogram, and cardiac magnetic resonance imaging scan revealed no abnormalities
March 2019	Exercise stress testing: Baseline ECG; PR = 206 ms, no fascicular block. At peak exercise PR =200 ms. During recovery paradoxical PR lengthening observed (PR = 280 ms)
July 2019	Electrophysiological study: Normal Atrio-His interval and PA intervals but abnormal HV = 84 ms
August 2019	Prophylactic DDDR PPM implanted

Case presentation

A 40-year-old Caucasian female, with MD1, was referred to our cardiomyopathy clinic following a 5-month history of atypical left-sided chest pain. MD1 was previously diagnosed following neurological examination which revealed myopathic facies, weakness of finger extension, and myotonia of hand closure. Analysis of the patient's DNA revealed one allele within the normal range and an expansion in the affected range (>50 CTG repeats) at the myotonic dystrophy 1 locus. A family pedigree diagram is depicted in *Figure 1*.

Both the patient's sister and mother aged 34 and 65 years, respectively, had been diagnosed with MD1 and had undergone prophylactic PPM implantation at a different institution. The sister's 14-year-old son also had genetically confirmed MD1. The patient's baseline electrocardiograms (ECGs) showed sinus rhythm, variable PR interval prolongation (206–220 ms), and intermittent left anterior fascicular block (LAFB). Routine blood tests, cardiac investigations including a 24-h ECG monitoring, echocardiogram, and a cardiac magnetic resonance imaging (MRI) scan were normal. We discussed the need for PPM implantation based on her prolonged PR interval and fascicular block. Of note, similar conduction abnormalities were present on an ECG performed by her General Practitioner 6 months prior to her current presentation.

To clarify the nature of her chest pain, the site and degree of her conduction abnormalities and guide our decision regarding device implantation, EST was performed as she retained good physical exercise capacity. Treadmill EST was performed according to the BRUCE protocol, achieving a maximum work level of METS: 7.10. The baseline ECG revealed sinus rhythm with a borderline first-degree AV block; PR = 206 ms, heart rate (HR) = 96 b.p.m. without fascicular block. No sustained tachy/bradyarrhythmias or relevant symptoms were observed before the test was stopped at 6 min due to fatigue. At peak exercise (HR = 157 b.p.m.), minimal PR interval shortening (PR = 200 ms) was observed and during the early recovery period (HR = 137 b.p.m.) paradoxical PR prolongation was observed with marked first-degree AV block (PR = 280 ms) that persisted throughout the recovery period (*Figure 2*). However, at the end of the recovery (5 min), the PR interval was seen to shorten to 216 ms.

Following the findings of EST, an EPS was performed to confirm the need for PPM implantation. The EPS revealed a prolonged HV interval of 84 ms (*Figure 2*), and the patient subsequently had a prophylactic DDDR PPM implanted. A ventricular tachycardia stimulation protocol was not performed due to the absence of ventricular arrhythmias on Holter monitoring and also because she had a normal cardiac MRI. She remains well at 24 months follow-up.

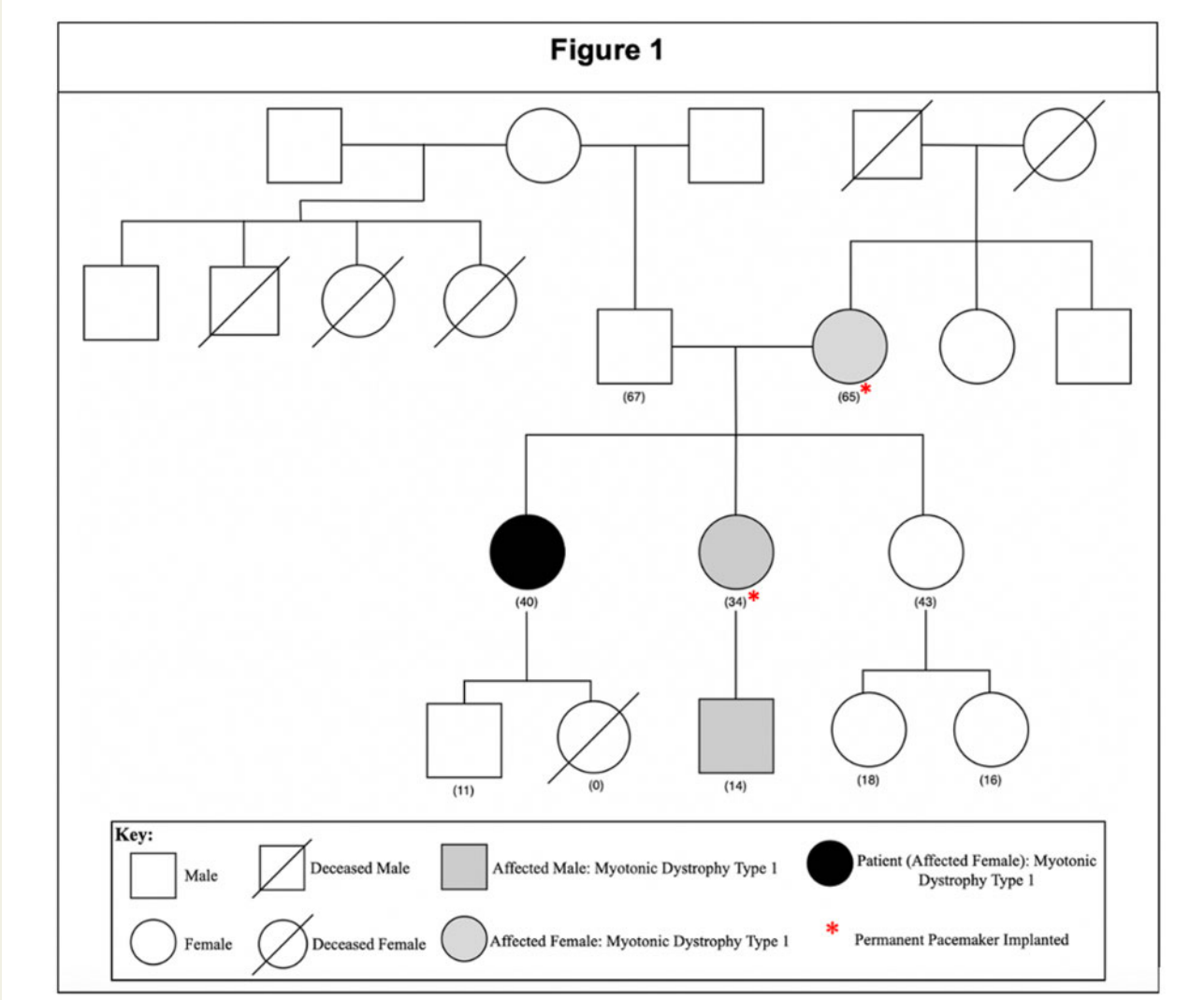

Figure 1 Family pedigree chart illustrating the prevalence of myotonic dystrophy type 1 in the patient's family. '(*x*)' denotes the individual's age. The patient's sister and mother aged 34 and 64 years, respectively, have had prophylactic permanent pacemaker implanted. The sister's son, aged 14 years also has myotonic dystrophy type 1.

Discussion

The progression of conduction system disease to high-grade AV block and ventricular tachyarrhythmias are thought to be the main mechanisms underlying SCD in MD1. Sudden cardiac death has been reported in 31% of MD1 patients and a risk-prediction score to determine the need for prophylactic pacemaker or defibrillator implantation has been proposed.[5]

Unfortunately, the need for primary prevention devices in MD1 relies on scoring systems based on data from non-randomized, observational studies underlying the need for tailored patient-centred interventions.[6,7]

Groh *et al.*[2] have reported the largest published observational study with 406 patients. It is worth noting that in this cohort, the presence of a significant ECG conduction abnormality and a clinical diagnosis of atrial tachyarrhythmia rather than clinical manifestation were the only independent predictors of sudden death underlying the need for electrophysiological surveillance.

Annual follow-up of patients without any specific symptoms of bradycardia is recommended with an ECG and 24-h ECG.[3] However, up to 32% of patients with MD1 have underlying conduction abnormalities present despite an apparently normal or borderline ECG, and consequently may go undetected.[8]

The presence of a PR interval >200 ms or a QRS complex >120 ms on ECG were found to be independent predictors of a prolonged HV interval (HV ≥ 70 ms) on EPS in a recent study of 100 MD1 patients.[9] Additionally, the mean time for conduction abnormalities to become identifiable on ECG in patients with MD1 was reported to be 5 ± 1 years in another study.[10] It is therefore questionable whether annual ECG monitoring alone is sufficient to identify conduction disease. Variable manifestation of conduction abnormalities as in our patient may lead to under detection of important

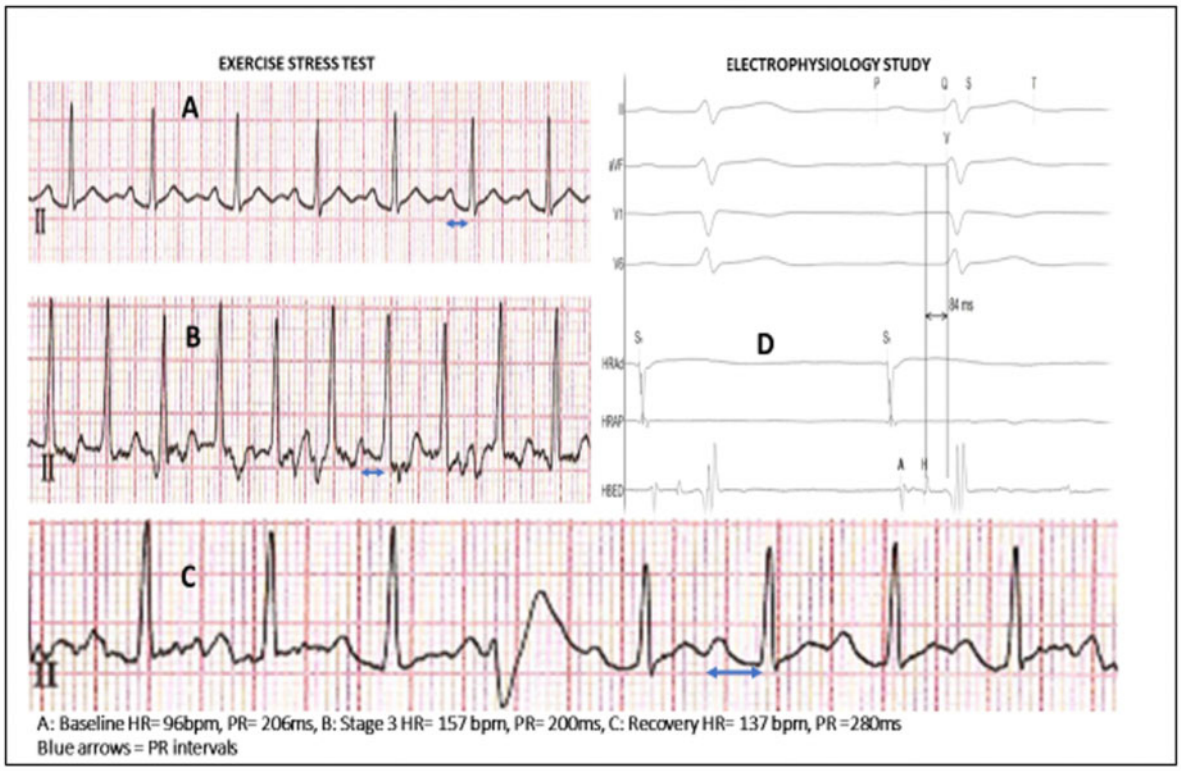

Figure 2 Exercise stress test demonstrating a PR interval of 206 ms at baseline (*A*), 200 ms at peak exercise (*B*), and 280 ms during the early recovery period (*C*). The findings on electrophysiology study (*D*) reveal a prolonged HV at 84 ms.

conduction disease. Although ambulatory ECG monitoring may aid in identifying intermittent conduction abnormalities, in one study, 18% of patients with MD1 were found to have apparently normal conduction on 24-h Holter monitoring, yet inducible arrhythmias were identified on EPS.[11]

In our patient, the ECG revealed minor PR interval prolongation (206 ms) with no fascicular block at the start of the EST, yet on an ECG performed 60 days prior, longer PR interval prolongation (223 ms) and LAFB were observed. At peak exercise, a withdrawal of the parasympathetic tone is expected to lead to PR interval shortening as was seen in our patient (HR = 157 b.p.m., PR = 200 ms). However, early in the recovery period (HR =137 b.p.m.), unexpected prolongation of the PR interval to 280 ms was observed before shortening of the PR interval to 216 ms at 5 min post-EST. Random alteration in our patient's autonomic tone cannot be excluded as an explanation for our findings. However, assessment of AV conduction post-exercise has been shown to improve prediction of cardiac death and arrhythmia risk in the general population and in inherited cardiac conditions.[12,13]

Electrophysiology studies remain the gold standard test for excluding significant conduction disease; indeed prophylactic PPM implantation guided by EPS has been reported to be superior to a non-invasive strategy in reducing the risk of sudden death in a large, observational, non-randomized study.[14] However, the invasive nature of an EPS limits its use as a screening tool for all patients with MD1. Exercise stress testing identifies functional abnormalities that manifest only during physiologic stress to the heart. For MD1 patients without good physical exercise capacity, the role for pharmacologic stress testing could be explored. In our patient with normal exercise tolerance, a stepwise approach to an EPS, guided by treadmill EST was used to unmask serious conduction disease.

In conclusion, EPS remains the gold standard diagnostic test to identify conduction abnormalities in patients with MD1. Exercise stress testing in MD1 patients who do not exhibit any specific symptoms of bradycardia could help identify patients who may benefit from invasive electrophysiological studies.

Lead author biography

Suliman Ahmad is a fourth-year medical student currently studying at Kings College London medical school. He has an active interest in cardiology research.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

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References

1. Udd B, Krahe R. The myotonic dystrophies: molecular, clinical, and therapeutic challenges. *Lancet Neurol* 2012;**11**:891–905.
2. Groh WJ, Groh MR, Saha C, Kincaid JC, Simmons Z, Ciafaloni E et al. Electrocardiographic abnormalities and sudden death in myotonic dystrophy type 1. *N Engl J Med* 2008;**358**:2688–2697.
3. Kusumoto FM, Schoenfeld MH, Barrett C, Edgerton JR, Ellenbogen KA, Gold MR et al. 2018 ACC/AHA/HRS Guideline on the evaluation and management of patients with bradycardia and cardiac conduction delay: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. *Circulation* 2019;**140**: e382–482.
4. Brignole M, Auricchio A, Baron-Esquivias G, Bordachar P, Boriani G, Breithardt OA et al. 2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy: the Task Force on cardiac pacing and resynchronization therapy of the European Society of Cardiology (ESC). Developed in collaboration with the European Heart Rhythm Association (EHRA). *Eur Heart J* 2013;**34**:2281–2329.
5. Wahbi K, Porcher R, Laforet P, Fayssoil A, Becane HM, Lazarus A et al. Development and validation of a newscoring system to predict survival in patients with myotonic dystrophy type 1. *JAMA Neurol* 2018;**75**:573–581.
6. Pelargonio G, Dello Russo A, Sanna T, de Martino G, Bellocci F. Myotonic dystrophy and the heart. *Heart* 2002;**88**:665–670.
7. Lazarus A, Varin J, Babuty D, Anselme F. R, Coste J, Duboc D. Long-term follow-up of arrhythmias in patients with myotonic dystrophy treated by pacing: a multicenter diagnostic pacemaker study. *J Am Coll Cardiol* 2002;**40**:1645–1652.
8. Merlevede K, Vermander D, Theys P, Legius E, Ector H, Robberecht W. Cardiac involvement and CTG expansion in myotonic dystrophy. *J Neurol* 2002;**249**: 693–698.
9. Joosten IBT, van Lohuizen R, den Uijl DW, Evertz R, de Greef BTA, van Engelen BGM et al. Electrocardiographic predictors of infrahissian conduction disturbances in myotonic dystrophy type 1. *EP Europace* 2020;**23**:298–304.
10. Brembilla-Perrot B, Luporsi JD, Louis S, Kaminsky P. Long-term follow-up of patients with myotonic dystrophy: an electrocardiogram every year is not necessary. *EP Europace* 2011;**13**:251–257.
11. Turner C, Hilton-Jones D. The myotonic dystrophies: diagnosis and management. *J Neurol Neurosurg Psychiatry* 2010;**81**:358–367.
12. Nieminen T, Verrier RL, Leino J, Nikus K, Lehtinen R, Lehtimäki T et al. Atrioventricular conduction and cardiovascular mortality: assessment of recovery PR interval is superior to pre-exercise measurement. *Heart Rhythm* 2010;**7**: 796–801.
13. Leong KMW, Ng FS, Shun-Shin MJ, Koa-Wing M, Qureshi N, Whinnett ZI et al. Non-invasive detection of exercise-induced cardiac conduction abnormalities in sudden cardiac death survivors in the inherited cardiac conditions. *EP Europace* 2021;**23**:305–312.
14. Wahbi K, Meune C, Porcher R, Bećane HM, Lazarus A, Laforêt P et al. Electrophysiological study with prophylactic pacing and survival in adults with myotonic dystrophy and conduction system disease. *JAMA* 2012;**307**:1292–1301.